World Health Organization

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Improving preterm birth outcomes

Executive summary

WHO recommendations on interventions to improve preterm birth outcomes

Introduction

Preterm babies are prone to serious illness or death during the neonatal period. Without appropriate treatment, those who survive are at increased risk of lifelong disability and poor quality of life. Complications of prematurity are the single largest cause of neonatal death and the second leading cause of deaths among children under the age of 5 years. Global efforts to further reduce child mortality demand urgent action to address preterm birth.

Infant death and morbidity following preterm birth can be reduced through interventions provided to the mother before or during pregnancy, and to the preterm infant after birth. Interventions can be directed at all women for primary prevention and reduction of the risk of preterm birth (e.g. smoking cessation programmes) or used to minimize the risk in pregnant women with known risk factors (e.g. progestational agents, cervical cerclage). However, the most beneficial set of maternal interventions are those that could improve survival chances and health outcomes of preterm infants when preterm birth is inevitable. These interventions are provided to the mother shortly before or during the birth process with the aim of overcoming immediate and future health challenges of the preterm infant, such as lung immaturity, susceptibility to infection, and neurological complications. Essential and additional care of the preterm newborn to prevent or treat potential complications is also critical to newborn survival without disability.

WHO's *Managing complications of pregnancy and childbirth: a guide for midwives and doctors* (published in 2000) and *Pocket book of hospital care for children* (published in 2013) have, respectively, provided guidance on maternal and newborn interventions that could improve the outcomes of preterm birth. In keeping with the WHO procedures for guideline development, these documents needed to be updated to include the current evidence-based practices and to respond to Member States' requests for guidance on controversial areas of practice. The present guideline is focused on interventions that could be provided during pregnancy, labour and during the newborn period with the aim of improving outcomes for preterm infants. Recommendations on interventions to prevent and reduce the risk of preterm birth or modify risk in at-risk pregnant women are outside the scope of this guideline.

Target audience

The primary audience for this guideline includes health-care professionals who are responsible for developing national and local health-care protocols and policies, as well as managers of maternal and child health programmes and policy-makers in all settings. The guideline will also be useful to those directly providing care to pregnant women and preterm infants, such as obstetricians, paediatricians, midwives, nurses and general practitioners. The information in this guideline will be useful for developing job aids and tools for pre- and in-service training of health workers to enhance their delivery of maternal and neonatal care relating to preterm birth.

Guideline development methods

The guideline was developed using standard operating procedures in accordance with the process described in the *WHO handbook for guideline development*. Briefly, these included (i) identification of priority questions and critical outcomes, (ii) retrieval of the evidence, (iii) assessment and synthesis of evidence, (iv) formulation of recommendations, and (v) planning for the dissemination, implementation, impact evaluation and updating of the guideline. The scientific evidence underpinning the recommendations was synthesized using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. Up-to-date systematic reviews were used to prepare evidence profiles for the priority questions. WHO then convened a Technical Consultation in May 2014 where an international group of experts – the Guideline Development Group (GDG) – formulated and approved the recommendations based on the evidence profiles. In November 2014, an online consultation of the GDG was conducted to review and revise the recommendations in the light of the findings of a large implementation trial of antenatal corticosteroids in low-resource countries.

Recommendations

The WHO Technical Consultation led to the adoption of 10 main recommendations (and 17 additional sub-recommendations) covering antenatal corticosteroids, tocolysis, magnesium sulfate, antibiotic prophylaxis, mode of preterm birth (for the mother) and Kangaroo mother care, plastic wraps, continuous positive airway pressure therapy, surfactant and oxygen therapy (for the newborn). For each recommendation, the quality of evidence was graded as "very low", "low", "moderate" or "high". The GDG qualified the direction and strength of each recommendation by considering the quality of evidence and other factors, including balance between benefits and harms, values and preferences of stakeholders, and the resource implications of the intervention. To ensure that each recommendation is correctly understood and applied in practice, the contributing experts provided additional remarks where needed. Guideline users should refer to these remarks, as well as the evidence summaries in the full version of the guideline, if there is any doubt as to the basis for any of the recommendations.

The recommendations on maternal and newborn interventions to improve health outcomes for the preterm infants are summarized in the table below. In accordance with WHO guideline development procedures, these recommendations will be constantly reviewed and updated following identification of new evidence, with major reviews and updates at least every five years. WHO welcomes suggestions regarding additional questions for inclusion in future updates of the guideline.

Summary list of WHO recommendations on interventions to improve preterm birth outcomes

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence[a]
Antenatal corticosteroids to improve newborn outcomes	**1.0.** Antenatal corticosteroid therapy is recommended for women at risk of preterm birth from 24 weeks to 34 weeks of gestation when the following conditions are met: • gestational age assessment can be accurately undertaken; • preterm birth is considered imminent; • there is no clinical evidence of maternal infection; • adequate childbirth care is available (including the capacity to recognize and safely manage preterm labour and birth); • the preterm newborn can receive adequate care if needed (including resuscitation, thermal care, feeding support, infection treatment and safe oxygen use).	**Strong recommendation** based on moderate-quality evidence for newborn outcomes and low-quality evidence for maternal outcomes
	1.1. For eligible women, antenatal corticosteroid should be administered when preterm birth is considered imminent within 7 days of starting treatment, including within the first 24 hours.	**Strong recommendation** based on low-quality evidence
	1.2. Antenatal corticosteroid therapy is recommended for women at risk of preterm birth irrespective of whether a single or multiple birth is anticipated.	**Strong recommendation** based on low-quality evidence
	1.3. Antenatal corticosteroid therapy is recommended in women with preterm prelabour rupture of membranes and no clinical signs of infection.	**Strong recommendation** based on moderate-quality evidence for newborn outcomes and low-quality evidence for maternal outcomes
	1.4. Antenatal corticosteroid therapy is not recommended in women with chorioamnionitis who are likely to deliver preterm.	**Conditional recommendation** based on very low-quality evidence
	1.5. Antenatal corticosteroid therapy is not recommended in women undergoing planned caesarean section at late preterm gestations (34–36^{+6} weeks).	**Conditional recommendation** based on very low-quality evidence
	1.6. Antenatal corticosteroid therapy is recommended in women with hypertensive disorders in pregnancy who are at risk of imminent preterm birth.	**Strong recommendation** based on moderate-quality evidence for newborn outcomes and low-quality evidence for maternal outcomes
	1.7. Antenatal corticosteroid therapy is recommended for women at risk of imminent preterm birth of a growth-restricted fetus.	**Strong recommendation** based on very low-quality evidence
	1.8. Antenatal corticosteroid therapy is recommended for women with pre-gestational and gestational diabetes who are at risk of imminent preterm birth, and this should be accompanied by interventions to optimize maternal blood glucose control.	**Strong recommendation** based on very low-quality evidence
	1.9. Either intramuscular (IM) dexamethasone or IM betamethasone (total 24 mg in divided doses) is recommended as the antenatal corticosteroid of choice when preterm birth is imminent.	**Strong recommendation** based on low-quality evidence
	1.10. A single repeat course of antenatal corticosteroid is recommended if preterm birth does not occur within 7 days after the initial dose, and a subsequent clinical assessment demonstrates that there is a high risk of preterm birth in the next 7 days.	**Conditional recommendation** based on moderate-quality evidence for newborn outcomes and low-quality evidence for maternal outcomes

[a] For recommendations related to maternal interventions, the rating of the quality of evidence applies to both the maternal and newborn outcomes where the quality of the evidence for the two is not separately presented.

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence[a]
Tocolytics for inhibiting preterm labour	**2.0.** Tocolytic treatments (acute and maintenance treatments) are not recommended for women at risk of imminent preterm birth for the purpose of improving newborn outcomes.	**Conditional recommendation** based on very low-quality evidence
Magnesium sulfate for fetal protection against neurological complications	**3.0.** The use of magnesium sulfate is recommended for women at risk of imminent preterm birth before 32 weeks of gestation for prevention of cerebral palsy in the infant and child.	**Strong recommendation** based on moderate-quality evidence
Antibiotics for preterm labour	**4.0.** Routine antibiotic administration is not recommended for women in preterm labour with intact amniotic membranes and no clinical signs of infection.	**Strong recommendation** based on moderate-quality evidence
	5.0. Antibiotic administration is recommended for women with preterm prelabour rupture of membranes.	**Strong recommendation** based on moderate-quality evidence
	5.1. Erythromycin is recommended as the antibiotic of choice for prophylaxis in women with preterm prelabour rupture of membranes.	**Conditional recommendation** based on moderate-quality evidence
	5.2. The use of a combination of amoxicillin and clavulanic acid ("co-amoxiclav") is not recommended for women with preterm prelabour rupture of membranes.	**Strong recommendation** based on moderate-quality evidence
Optimal mode of delivery	**6.0.** Routine delivery by caesarean section for the purpose of improving preterm newborn outcomes is not recommended, regardless of cephalic or breech presentation.	**Conditional recommendation** based on very low-quality evidence
Thermal care for preterm newborns	**7.0.** Kangaroo mother care is recommended for the routine care of newborns weighing 2000 g or less at birth, and should be initiated in health-care facilities as soon as the newborns are clinically stable.	**Strong recommendation** based on moderate-quality evidence
	7.1. Newborns weighing 2000 g or less at birth should be provided as close to continuous Kangaroo mother care as possible.	**Strong recommendation** based on moderate-quality evidence
	7.2. Intermittent Kangaroo mother care, rather than conventional care, is recommended for newborns weighing 2000 g or less at birth, if continuous Kangaroo mother care is not possible.	**Strong recommendation** based on moderate-quality evidence

Maternal interventions	Recommendations	Strength of recommendation and quality of the evidence[a]
Thermal care for preterm newborns (*continued*)	7.3. Unstable newborns weighing 2000 g or less at birth, or stable newborns weighing less than 2000 g who cannot be given Kangaroo mother care, should be cared for in a thermo-neutral environment either under radiant warmers or in incubators.	**Strong recommendation** based on very low-quality evidence
	7.4. There is insufficient evidence on the effectiveness of plastic bags/wraps in providing thermal care for preterm newborns immediately after birth. However, during stabilization and transfer of preterm newborns to specialized neonatal care wards, wrapping in plastic bags/wraps may be considered as an alternative to prevent hypothermia.	**Conditional recommendation** based on low-quality evidence
Continuous positive airway pressure for newborns with respiratory distress syndrome	**8.0.** Continuous positive airway pressure therapy is recommended for the treatment of preterm newborns with respiratory distress syndrome.	**Strong recommendation** based on low-quality evidence
	8.1. Continuous positive airway pressure therapy for newborns with respiratory distress syndrome should be started as soon as the diagnosis is made.	**Strong recommendation** based on very low-quality evidence
Surfactant administration for newborns with respiratory distress syndrome	**9.0.** Surfactant replacement therapy is recommended for intubated and ventilated newborns with respiratory distress syndrome.	**Conditional recommendation** (only in health-care facilities where intubation, ventilator care, blood gas analysis, newborn nursing care and monitoring are available) based on moderate-quality evidence
	9.1. Either animal-derived or protein-containing synthetic surfactants can be used for surfactant replacement therapy in ventilated preterm newborns with respiratory distress syndrome.	**Conditional recommendation** (only in health-care facilities where intubation, ventilator care, blood gas analysis, newborn nursing care and monitoring are available) based on moderate-quality evidence
	9.2. Administration of surfactant before the onset of respiratory distress syndrome (prophylactic administration) in preterm newborns is not recommended.	**Strong recommendation** based on low-quality evidence
	9.3. In intubated preterm newborns with respiratory distress syndrome, surfactant should be administered early (within the first 2 hours after birth) rather than waiting for the symptoms to worsen before giving rescue therapy.	**Conditional recommendation** (only in health-care facilities where intubation, ventilator care, blood gas analysis, newborn nursing care and monitoring are available) based on low-quality evidence
Oxygen therapy and concentration for preterm newborns	**10.0.** During ventilation of preterm babies born at or before 32 weeks of gestation, it is recommended to start oxygen therapy with 30% oxygen or air (if blended oxygen is not available), rather than with 100% oxygen.	**Strong recommendation** based on very low-quality evidence
	10.1. The use of progressively higher concentrations of oxygen should only be considered for newborns undergoing oxygen therapy if their heart rate is less than 60 beats per minute after 30 seconds of adequate ventilation with 30% oxygen or air.	**Strong recommendation** based on very low-quality evidence

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For more information, please contact:

Department of Reproductive Health and Research
World Health Organization
Avenue Appia 20, CH-1211 Geneva 27, Switzerland
E-mail: reproductivehealth@who.int

www.who.int/reproductivehealth

Department of Maternal, Newborn, Child & Adolescent Health
World Health Organization
Avenue Appia 20, CH-1211 Geneva 27, Switzerland
E-mail: mncah@who.int

www.who.int/maternal_child_adolescent

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